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Patient-reported conformity of informed consent procedures and participation in clinical research

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Summary

Background: There is growing evidence that the quality of informed consent in clinical research is often sub-optimal.
Aims: To explore the conformity of patient recruitment with recommended informed consent procedures among patients who were invited to participate in a clinical study at a general teaching hospital, and to examine the association between consent procedures and the patients' decision to participate.
Design and Methods: All inpatients discharged during a 1-month period were invited to complete a mailed survey in which they reported whether they were invited to participate in a study and whether 13 recommended elements of informed consent actually occurred.
Results: Among 1303 respondents, 265 (20.3%) reported that they had been invited to participate in a study, and 191 (72.1%) accepted. While the majority of potential participants were fully informed about practical issues related to the study (e.g. what their participation would consist in), <50% were informed of possible risks or benefits, and only 20% about the origin of the study funds. Only 60% reported satisfactory answers to items assessing the overall information process (e.g. explanations were easy to understand). Older and sicker patients reported lower levels of conformity with informed consent procedures, as did patients who refused to participate in a study.
Conclusions: Our results confirm that informed consent procedures fail to meet standards for many patients. In particular, consent information should be adapted to the needs of older and sicker patients. Improving the quality of informed consent may increase patients' participation in clinical research.

Introduction

Patient participation in clinical research is indispensable for the development of evidence-based medicine. Agreeing to take part in a study is an altruistic act[1] that may entail certain risks. To protect research subjects from potential harm[2] and to ensure that they reach an autonomous and informed decision,[3] World Health Organization (WHO) has adopted an international framework of principles for informed consent in research (Declaration of Helsinki[4]). Based on this framework, regulatory authorities have further developed official guidelines such as the ICH guideline for Good Clinical Practice.[5] These recommendations and guidelines describe information and explanations that investigators are required to provide during the informed consent discussion and in the written consent form.[4,5] Namely, potential participants should be informed of the purpose and process of the study, their right to abstain and to withdraw at any time, and of possible benefits, risks or drawbacks related to their participation. They should also be informed of the sources of funding of the study, as of any other

possible cause of conflict of interest.[4] Finally, investigators should not only disclose information, but also ensure that participants reach proper understanding, particularly by using non-technical and practical language, adapted to each participant's needs and impairments, so that they make an informed and decision.[3–5]

However, the quality of informed consent in real life is often sub-optimal, both in terms of conformity with recommended practices, and in terms of participants' understanding of study-related information.[6–15] Available evidence in this domain is fragmented. Most studies to date have assessed the quality of informed consent in narrow clinical contexts, such as oncology,[7,8] cardio-vascular medicine[9,10] or gynecology.[11,12] Furthermore, previous studies have focused on consent in clinical trials,[13–15] disregarding other types of research.

Another limitation of existing studies is that few have compared subjects who accepted to participate and those who refused.[16,17] The latter may be less well-informed about the study, perhaps because they found consent information hard to understand, with the potential implication that they may not have given an informed refusal.[6] Further understanding of the adequacy of informed consent in real clinical setting and of its impact on participation is critical, since most interventions to improve patient understanding have had only limited success,[18,19] as have most strategies to improve recruitment.[20]

In this study, we examined the conformity of informed consent with recommended procedures among all potential participants in any clinical research project during their stay at a large public teaching hospital. Our secondary aims were: (i) to assess how many inpatients were invited to participate and whether there was any sub-group that was more or less likely to be invited; (ii) to examine the association between adequacy of informed consent and the patients' decision to participate in the study.

Methods

Study design and setting

Data were obtained as part of a routine patient opinion survey at Geneva University Hospitals, in Geneva, Switzerland. This teaching hospital network includes acute care, geriatric, psychiatric and rehabilitation facilities, totalling 2096 beds and about 47 000 inpatient admissions annually. Potential participants were all adult patients hospitalized for >24 h and discharged either to their home or to a nursing facility between 15 September and 15 October 2005. The initial sample was identified through the administrative database. The survey package was sent by mail to 2469 individuals 4–8 weeks after discharge, with up to two reminders sent during the next 3 months. During data collection, we excluded patients who had moved away, died, stated that they were too sick to fill in the questionnaire, or did not speak French. As quality assessment projects that carry minimal risk, these surveys[21,22] are exempted from full review by the hospital research ethics committee.

Study variables

The core of the questionnaire was the Picker patient experience survey.[23] This questionnaire includes mostly questions on various aspects of care received at the hospital. An example is an item that asks the patient whether he or she 'could understand the doctors' explanations', with possible answers 'yes, always', 'yes, sometimes' or 'no'. Only this item from the Picker survey was analyzed in this article. Respondents were also asked to report demographic variables (age, sex, nationality, level of education) and their perceived general health (item from the SF-36 questionnaire[24,25]).

The main variables in this analysis related to patients' involvement in clinical research. First, we asked respondents if they had been invited to participate in a study during their hospital stay, and whether they accepted or refused to participate. Second, we asked patients who were invited to participate in a study to report whether fundamental aspects of the informed consent process occurred. We assessed 13 specific aspects of the informed consent procedure as outlined in the Declaration of Helsinki[4] and in the International Conference on Harmonization (ICH) Guideline for Good Clinical Practice.[5] We were also inspired by the previous studies that assessed the quality of informed consent in specific clinical contexts.[10,12,26] Specifically, we asked patients to state whether they were informed of: the purpose of the study, what their participation would consist in, possible benefits, risks or drawbacks, their right to abstain and to withdraw at any time, and the origin of the study funds. To assess the information process globally, we also asked them if they had the opportunity to ask questions, if the explanations as well as written information were easy to understand, and finally if they received enough information and had enough time to decide. As we surveyed potential participants in studies of various designs, we did not assess understanding of particular features of

trials, such as randomization, the unproven nature of the treatment or the uncertainty of benefits to themselves.[6] To facilitate completion of the questionnaire we formulated the questions in keeping with the format of Picker survey items, with possible answers being: 'yes, completely – (yes, to some extent) – no'. One additional item explored the respondents' overall attitude toward clinical research, by asking whether it is 'justified for doctors to ask patients to contribute to producing knowledge that will be useful to others'.

Data analysis

We started by comparing respondents who completed the section exploring involvement in clinical research to those who skipped the section but filled out the rest of the questionnaire.

Then, we analyzed the proportion of patients who reported that they had been invited to participate in clinical research across sub-groups of respondents. Among the patients who were invited, we determined the frequency of conformity with each aspect of the informed consent process.

To capture the overall conformity with recommendations, we constructed a global conformity score, as follows:

$$\text{Conformity score} = \frac{\sum \text{'Yes, completely'} \times 1 + \text{'Yes, to some extent'} \times 0.5}{\text{Number of items}} \times 100$$

The score was computed among respondents who answered at least 7 of the 13 relevant items, and ranged from 0 (lowest possible conformity) to 100 (full conformity on all items). Then, we explored the overall level of reported conformity across sub-groups of respondents.

Finally, we analyzed the proportion of patients who accepted to participate in research according to the conformity of each aspect of the informed consent. We built a multiple logistic regression model to identify aspects that were independently associated with participation. We used a forward modeling procedure, guided by the analyst, where only statistically significant aspects were included in the model. Data were analyzed using SPSS 15.0 software.

Results

Sample characteristics

During data collection, we excluded 265 patients from the initial sample because they moved away, died, did not speak French, of were too sick to respond. Of the 2204 eligible patients, 1432 (65%) returned completed questionnaires, and 1303 (91% of 1432) filled out the section exploring involvement in clinical research. Respondents to this section were younger than the 129 non-respondents (mean age 53 vs. 62 years, $P < 0.001$), had shorter hospital stays (mean 9.5 vs. 13.7 days, $P = 0.017$), had higher level of education (34.1% vs. 14.3% attended university or a professional school, $P < 0.001$), and reported better self-perceived health status (32.6% vs. 16.9% rated their health as excellent of very good, $P = 0.002$). Distributions of others patients' covariates were similar in the two groups.

Respondent characteristics are shown in Table 1, column 1. Few patients from the department of geriatrics were included due to an error in the administrative patient database. Nevertheless, many older patients were hospitalized in internal medicine, where 43% of patients were >70 years.

Proportion of patients invited to participate in clinical research

Among 1303 respondents, 265 (20.3%) reported that they had been invited to participate in a clinical research project. Distributions of invited patients were fairly homogenous across sub-groups of respondents, and no particular group was completely ignored by investigators (Table 1, column 2). However, younger patients were more often invited to participate in research than older patients, and differences between departments were also statistically significant.

Conformity with recommended informed consent procedures

About 75% of the patients invited to participate in a study reported that they were completely informed on practical issues, such as the purpose of the study, the right to withdraw at any time and what their participation would consist in, and 90% were informed that participation was not obligatory (Table 2, column 2). However, <50% reported that they were completely informed of possible benefits, risks or drawbacks and only 20% reported that they were informed of the origin of the study funds. As for the items that addressed the information process globally, ~60% of the respondents reported that they had the opportunity to ask questions, that the explanations were easy to understand and that they received enough information and had enough time to decide, and only 50% reported that written information was completely understandable.

Table 1 Proportion of patients invited in clinical research and conformity with informed consent procedures across sub-groups of respondents

	Respondents	Patients invited to participate in clinical research			Conformity score of informed consent[a]	
	N[b] (%)	N[c]	Percentage of respondents	P-value	Mean (SD)	P-value[d]
Sex				0.163		0.636
Female	761 (58.5)	165	21.7		68.6 (25.2)	
Male	540 (41.5)	100	18.5		66.2 (27.2)	
Age (years)				0.014		0.005
18–44	508 (39.0)	124	24.4		71.5 (21.6)	
45–64	379 (29.1)	69	18.2		70.7 (27.4)	
≥65	414 (31.8)	72	17.4		57.5 (29.5)	
Nationality				0.069		0.836
Swiss	682 (53.0)	145	21.3		69.2 (23.6)	
European	403 (31.7)	66	16.4		66.8 (29.0)	
Other countries	188 (14.8)	44	23.4		64.9 (27.8)	
Level of education				0.071[e]		0.192
Compulsory school	277 (22.2)	51	18.4		63.2 (28.2)	
Apprenticeship	406 (32.6)	73	18.0		66.8 (27.7)	
Secondary school	138 (11.1)	29	21.0		69.6 (23.0)	
Professional school	185 (14.8)	37	20.0		64.9 (24.0)	
University	240 (19.3)	58	24.2		75.0 (20.9)	
Length of hospital stay (days)				0.301[e]		0.306
≤10	1005 (77.2)	200	19.9		69.4 (24.6)	
11–15	230 (17.7)	48	20.9		61.7 (29.9)	
>15	66 (5.1)	17	25.8		62.8 (28.8)	
Department of hospitalization				<0.001		0.034
Medicine	257 (19.8)	62	24.1		67.6 (26.1)	
Surgery	452 (34.7)	57	12.6		64.1 (30.8)	
Neurosciences	207 (15.9)	30	14.5		58.1 (29.9)	
Genecology–obstetrics	294 (22.6)	94	32.0		74.0 (20.7)	
Geriatrics	31 (2.4)	9	29.0		51.1 (22.4)	
Psychiatry	60 (4.6)	13	21.7		66.4 (24.9)	
Perceived health status				0.371		<0.001
Excellent/very good	407 (32.6)	88	21.6		76.5 (21.7)	
Good/fair/poor	843 (67.4)	164	19.5		63.2 (26.1)	

[a]Score from 0 to 100 (maximal conformity, see text), mean = 67.7, SD = 25.9, median = 73.1.
[b]The total is different from 1303 because of missing values ranging from 0.2% to 4.4%.
[c]The total may be different from 265 because of missing values ranging from 0.0% to 6.4%.
[d]Non-parametrical test: Mann–Whitney test for comparison of two groups and Kruskal–Wallis test for more than two groups.
[e]Test for linear trend.

The mean conformity score based on all 13 items was 67.7 (SD = 25.9, quartiles = 53.8–73.1–88.4) on a scale from 0 to 100. It was computed for the 239 (90.2%) patients who reported valid answers for more than seven conformity items. Three variables were significantly associated with this score: age, self-perceived health status and hospital department (Table 1, column 3). On average, patients >65 years reported lower conformity—by about half a standard deviation—than younger patients, as did respondents that rated their health as 'good, fair or poor' instead of 'excellent or very good'.

Informed consent and decision to participate in a study

Of the 265 patients who were invited to participate in a research study, 191 (72.1%, or 14.7% of all respondents) reported that they agreed to participate, while 53 (20%) refused, and 21 (7.9%) did not answer this question. Overall conformity with recommended informed consent procedures was associated with participation in the study (mean score 72.6 among those who accepted vs. 51.9 among those who refused, $P < 0.001$). However,

Table 2 Patient-reported conformity with 13 elements of the informed consent procedure and association with acceptance to participate in a study

Items of the questionnaire assessing conformity of informed consent procedure	*N*[a]	Column percentage	Row percentage who accepted to participate[b] (*P*-value)
Purpose of the study was explained			(<0.001)
Yes, completely	184	75.1	85.9
Yes, to some extent	41	16.7	84.6
No	20	8.2	25.0
Missing, *n* = 20			
What your participation would consist in was explained			(<0.001)
Yes, completely	180	74.1	87.4
Yes, to some extent	39	16.0	80.0
No	24	9.9	33.3
Missing, *n* = 22			
Informed of possible benefits			(0.712)
Yes, completely	112	48.3	81.7
Yes, to some extent	43	18.5	78.6
No	77	33.2	76.7
Missing, *n* = 33			
Informed of drawbacks and obligations			(0.089)
Yes, completely	113	50.0	85.7
Yes, to some extent	43	19.0	70.7
No	70	31.0	77.3
Missing, *n* = 39			
Informed of possible risks			(0.142)
Yes, completely	110	49.8	83.3
Yes, to some extent	35	15.8	67.6
No	76	34.4	79.5
Missing, *n* = 44			
Informed that participation was not obligatory			(<0.001)
Yes	219	89.0	85.5
No	27	11.0	26.1
Missing, *n* = 19			
Informed of your right to withdraw at any time			(0.001)
Yes	174	74.4	85.3
No	60	25.6	64.9
Missing, *n* = 31			
Informed of the origin of funding			(0.215)
Yes	52	22.4	73.1
No	180	77.6	81.0
Missing, *n* = 33			
Had the opportunity to ask questions			(0.006)
Yes, completely	136	57.6	85.0
Yes, to some extent	41	17.4	80.5
No	59	25.0	64.3
Missing, *n* = 29			
Explanations were easy to understand			(<0.001)
Yes, completely	144	62.3	86.6
Yes, to some extent	69	29.9	76.1
No	18	7.8	41.2
Missing, *n* = 34			
Written information was easy to understand			(0.001)
Yes, completely	118	49.2	89.0
Yes, to some extent	51	21.3	74.5
No or did not receive any written information	71	29.6	66.7
Missing, *n* = 25			
Received enough information to decide			(<0.001)
Yes, completely	157	65.7	85.4
Yes, to some extent	48	20.1	89.4
No	34	14.2	35.5
Missing, *n* = 26			
Had enough time to decide			(<0.001)
Yes, completely	148	61.9	88.5
Yes, to some extent	47	19.7	77.8
No	44	18.4	51.2
Missing, *n* = 26			

[a]Among 265 patients invited to participate, 10 patients showed missing value for this entire section.
[b]There were 21 missing answers regarding decision to participate.

Table 3 Independent predictors of participation in clinical research

	Adjusted OR (*P*-value)	95% CI
Purpose of the study was explained	(0.001)	
Yes, completely	10.41	(2.77–39.16)
Yes, to some extent	10.44	(2.25–48.45)
No	Reference	–
Informed that participation was not obligatory	(<0.001)	
Yes	10.39	(3.18–40.00)
No	Reference	–
Informed of the origin of funding	(0.005)	
Yes	0.29	(0.12–0.69)
No	Reference	–

not all items were specifically associated with participation (Table 2, column 3). While information on practical issues was strongly associated with higher participation rates, information about possible benefits, risks or drawbacks was not. All items assessing the overall information process were associated with participation.

To understand if these associations were specific, we examined study participation in relation to patient reports of whether doctors' explanations about health care (not about research) were completely understandable, an item from the Picker survey. This item was not associated with the decision to participate in research (the proportion of respondents that accepted to participate was of 76.1% among those who found doctors' explanation completely understandable vs. 77.4% among those who did not).

In multivariate analysis, three items remained significantly associated with participation (Table 3), and accounted for one-third of the variance in participation (Nagelkerke $R^2 = 0.32$). Unexpectedly, having received information about the origin of the study funds had a negative impact on acceptance to enroll in a study. Further adjustment for the respondent's general attitude toward research did not change these results (data not shown).

Discussion

Twenty percent of former inpatients at a public teaching hospital reported that they had been invited to participate in clinical research during their hospital stay, and most of them (72%) agreed to participate. Although all sub-groups of patients were approached by investigators, older patients were less often invited. Potential participants in research did not report a uniformly high level of conformity with each of 13 recommended aspects of informed consent. While information about practical aspects and the voluntary nature of research were acceptable, information about risks, benefits and the origin of funding was poor. As for the efforts that were made to ensure proper understanding, only ~60% of respondents reported satisfactory answers. Furthermore, the overall conformity with informed consent procedures varied with age and self-perceived health status, with the older and sicker patients reporting a less desirable process than others. Finally, several aspects of informed consent were associated with the actual decision to participate, as those who declined participation reported systematically lower levels of conformity with informed consent procedures. In multivariate analysis, information about the purpose of the study and the right to decline participation were associated with higher participation rates, while information about the origin of funding had the opposite effect.

Proportion of patients invited or involved in clinical research

About one out of the seven respondents stated that they participated in a study during their hospital stay. We were not able to verify the accuracy of these reports. Our estimate is similar to findings of a previous study among outpatients of 16 oncology and cardiology clinics.[27] Based on independent record review, this study found strong evidence of research participation for 16% (302/1882) of outpatients, and positive and negative predictive values of patient reports of participation both reached 94%.

An important issue about patient recruitment in clinical trials is the possible under-representation of socio-demographic sub-groups such as older people, women or ethnic minorities.[28] We found no major disparities of this kind. However, like others, we found that older patient were less likely

to report being recruited.[29] This could be a true finding, or an example of information bias, as older patients may lack a clear understanding of whether they were enrolled in research.[30]

Conformity with recommendations on informed consent

Our findings about practical information, such as the purpose of the study and the voluntary nature of research, are similar to those of previous studies of specific trials.[7,13,31] However, our patients reported a less-satisfactory information process than others. For example, in a study of 207 patients with cancer who were recently enrolled in a clinical trial, 93% reported that they had had sufficient opportunity to ask questions, 86% reported that the consent form was easy to understand and 87% said they had enough time to learn about the trial.[7] In contrast, only ~50–60% of our respondents reported similar answers to these items.

The patients we surveyed were invited to participate in various types of studies, not just randomized trials, and were likely older or more severely ill than outpatients recently enrolled in specific clinical trials.[7,13,27,31,32] Older and sicker patient report lower levels of adequacy of the informed consent procedure, as we and others[30,31] have observed. One possibility is that older and sicker patients were enrolled in studies that had less appropriate practices in place. Alternatively, such patients may suffer from discrimination, independently of the nature of the study. For instance, study information may be tailored to younger and healthier people. These results emphasize the importance of adapting consent information to patients' needs and impairments, especially to more vulnerable sub-groups of patients, so that they can also make an informed decision.

Adequacy of informed consent and decision to participate

In contrast with most previous work, we obtained information from patients who refused to participate in research. Those who refused reported significantly lower levels of conformity with informed consent procedures. This raises a red flag, as these potential participants may not have given an informed refusal. Alternatively, those who declined participation may remember less well the recruitment process than those who agreed to participate. However, we believe that information bias is an unlikely explanation, given the strength and the specificity of the observed associations.

Indeed, not all aspects of the conformity with recommendations were associated with participation. For instance, the decision to participate was only marginally affected by information about possible risks or drawbacks. This is reassuring, since these aspects of a study are often emphasized in patient information documents.[3]

Another interesting finding is the negative impact of financial disclosure on participation in multivariate analysis. This association was not observed in univariate analysis, probably because it was confounded by the positive association between overall conformity on the other items and the decision to participate. Indeed, patients who reported that they were informed of study funds also reported higher levels of overall conformity on the other items (85.0 vs. 66.2, $P < 0.001$), which probably masked the negative impact of financial disclosure.

Investigators are expected to disclose any potential conflict of interest, including sources of funding,[4] in order to fully inform research subjects and strengthen the trust relationship between the public and the scientific community.[33] However, there is controversy about the impact of such disclosure on recruitment. Others have found that financial disclosure is unlikely to affect the decision to participate in a hypothetical trial.[34] Information about the origin of funding may reduce participation in clinical settings, if patients generally considered only altruistic motives of researchers and were unaware of commercial implications. On the other hand, financial disclosure may have occurred more often in situations that investigators considered as possibly problematic (e.g. funding by private industry),[35] hence the negative impact on patient participation. Both explanations raise the ethical problem of weighing recruitment considerations and the duty to fully inform potential participants.

Limitation and strengths

The main limitation of the study is the lack of independent verification of patients' reports. To protect the privacy of respondents in the satisfaction survey, we did not have access to their medical records. However, previous studies[27] suggest that the patients' recall of research is generally good. As for any study based on self-reports, social desirability bias and recall bias may also apply to our results.

The moderate response rate raises the possibility of selection bias. This would probably inflate reported levels of conformity, as respondents to the research section of the survey tented to be younger, more educated and in better health. However, an analysis of a similar survey at the same hospital showed that non-response bias was modest, at

least for the Picker patient opinion survey.[22] On balance, as discussed above, we believe our results are internally valid. However, only one hospital was involved, so that the generalizability of our findings is questionable.

The main strengths of our study are that we tested a wide array of recommended elements for informed consent, and that we included both patients who accepted and who refused to participate in clinical research, in contrast with previous studies. We were thus able to explore how adequacy of informed consent may influence patients' decision to participate. However, we did not consider other important factors that may impact on their acceptance, such as attitudes toward clinical research, perceived risks and expected benefits of their participation or the burden it may entail.[36,37] Indeed, conformity with informed consent procedure explained only one-third of the variance in participation in our multivariate analysis.

Finally, we surveyed a large unselected sample of potential participants, in contrast, with previous research that assessed the quality of informed consent in narrow clinical contexts and focused on consent in clinical trials. Thus our study may yield a wider assessment of conformity with informed consent procedures in real clinical settings. At the same time, this is also a limitation, since our sample is heterogeneous and we were not able to relate patients' reports to actual informed consent documents.

Conclusion

Our results confirm that the informed consent process for research studies is imperfect, particularly regarding information on risks or financial disclosure. Our results also call attention to the need to adapt consent information to vulnerable sub-groups of patients. Improvement of informed consent may contribute to increase participation in research, since non-participants reported a lower quality of the consent process, in addition to enabling potential participants to reach an informed decision.

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References

1. Madsen S, Holm S, Riis P. Ethical aspects of clinical trials: the attitudes of the public and out-patients. *J Intern Med* 1999; **245**:571–9.
2. Steinbrook R. Improving protection for research subjects. *N Engl J Med* 2002; **346**:1425–30.
3. Jefford M, Moore R. Improvement of informed consent and the quality of consent documents. *Lancet Oncol* 2008; **9**:485–93.
4. World Medical Association. Declaration of Helsinki: ethical principles for medical research involving human subjects. *JAMA* 2000; **284**:3043–5.
5. ICH Harmonised Tripartite Guideline, Guideline for Good Clinical Practice. [http://www.ich.org/LOB/media/MEDIA482.pdf] Accessed 6 January 2010.
6. Robinson EJ, Kerr CE, Stevens AJ, Lilford R, Braunholtz D, Edwards S, *et al.* Lay public's understanding of equipoise and randomisation in randomised controlled trials. *Health Technol Assess* 2005; **9**:1–192, iii–iv.
7. Joffe S, Cook EF, Cleary PD, Clark JW, Weeks JC. Quality of informed consent in cancer clinical trials: a cross-sectional survey. *Lancet* 2001; **358**:1772–7.
8. Gotay CC. Perceptions of informed consent by participants in a prostate cancer prevention study. *Cancer Epidemiol Biomarkers Prev* 2001; **10**:1097–9.
9. Gammelgaard A, Mortensen OS, Rossel P. Patients' perceptions of informed consent in acute myocardial infarction research: a questionnaire based survey of the consent process in the DANAMI-2 trial. *Heart* 2004; **90**:1124–8.
10. Yuval R, Halon DA, Merdler A, Khader N, Karkabi B, Uziel K, *et al.* Patient comprehension and reaction to participating in a double-blind randomized clinical trial (ISIS-4) in acute myocardial infarction. *Arch Intern Med* 2000; **160**:1142–6.
11. Fortney JA. Assessing recall and understanding of informed consent in a contraceptive clinical trial. *Stud Fam Plann* 1999; **30**:339–46.
12. Lynoe N, Sandlund M, Dahlqvist G, Jacobsson L. Informed consent: study of quality of information given to participants in a clinical trial. *Br Med J* 1991; **303**:610–3.
13. Durand-Zaleski IS, Alberti C, Durieux P, Duval X, Gottot S, Ravaud Ph, *et al.* Informed consent in clinical research in France: assessment and factors associated with therapeutic misconception. *J Med Ethics* 2008; **34**:e16.
14. Griffin JM, Struve JK, Collins D, Liu A, Nelson DB, Bloomfield HE. Long term clinical trials: how much information do participants retain from the informed consent process? *Contemp Clin Trials* 2006; **27**:441–8.
15. Stryker JE, Wray RJ, Emmons KM, Winer E, Demetri G. Understanding the decisions of cancer clinical trial participants to enter research studies: factors associated with informed consent, patient satisfaction, and decisional regret. *Patient Educ Couns* 2006; **63**:104–9.

16. Leach A, Hilton S, Greenwood BM, Manneh E, Dibba B, Wilkins A, *et al.* An evaluation of the informed consent procedure used during a trial of a Haemophilus influenzae type B conjugate vaccine undertaken in The Gambia, West Africa. *Soc Sci Med* 1999; **48**:139–48.
17. Lovegrove E, Rumsey N, Harcourt D, Cawthorn SJ. Factors implicated in the decision whether or not to join the tamoxifen trial in women at high familial risk of breast cancer. *Psychooncology* 2000; **9**:193–202.
18. Flory J, Emanuel E. Interventions to improve research participants' understanding in informed consent for research: a systematic review. *JAMA* 2004; **292**:1593–601.
19. Edwards SJ, Lilford RJ, Thornton J, Hewison J. Informed consent for clinical trials: in search of the ''best'' method. *Soc Sci Med* 1998; **47**:1825–40.
20. Mapstone J, Elbourne D, Roberts I. Strategies to improve recruitment to research studies. *Cochrane Database Syst Rev* 2007, Issue 2:MR000013.
21. Agoritsas T, Bovier PA, Perneger TV. Patient reports of undesirable events during hospitalization. *J Gen Intern Med* 2005; **20**:922–8.
22. Perneger TV, Chamot E, Bovier PA. Nonresponse bias in a survey of patient perceptions of hospital care. *Med Care* 2005; **43**:374–80.
23. Jenkinson C, Coulter A, Bruster S. The Picker Patient Experience Questionnaire: development and validation using data from in-patient surveys in five countries. *Int J Qual Health Care* 2002; **14**:353–8.
24. Jenkinson C, Stewart-Brown S, Petersen S, Paice C. Assessment of the SF-36 version 2 in the United Kingdom. *J Epidemiol Commun Health* 1999; **53**:46–50.
25. Leplege A, Ecosse E, Verdier A, Perneger TV. The French SF-36 Health Survey: translation, cultural adaptation and preliminary psychometric evaluation. *J Clin Epidemiol* 1998; **51**:1013–23.
26. Joffe S, Cook EF, Cleary PD, Clark JW, Weeks JC. Quality of informed consent: a new measure of understanding among research subjects. *J Natl Cancer Inst* 2001; **93**:139–47.
27. Sugarman J, Kass NE, Goodman SN, Perentesis P, Fernandes P, Faden RR. What patients say about medical research. *IRB* 1998; **20**:1–7.
28. Bartlett C, Doyal L, Ebrahim S, Davey P, Bachmann M, Egger M, *et al.* The causes and effects of socio-demographic exclusions from clinical trials. *Health Technol Assess* 2005; **9**:iii–iv, ix–x, 1–152.
29. Bugeja G, Kumar A, Banerjee AK. Exclusion of elderly people from clinical research: a descriptive study of published reports. *Br Med J* 1997; **315**:1059.
30. Sugarman J, McCrory DC, Hubal RC. Getting meaningful informed consent from older adults: a structured literature review of empirical research. *J Am Geriatr Soc* 1998; **46**:517–24.
31. Schaeffer MH, Krantz DS, Wichman A, Masur H, Reed E, Vinicky JK. The impact of disease severity on the informed consent process in clinical research. *Am J Med* 1996; **100**:261–8.
32. Ferguson PR. Patients' perceptions of information provided in clinical trials. *J Med Ethics* 2002; **28**:45–8.
33. AAMC Task Force on Financial Conflicts of Interest in Clinical Research. Protecting subjects, preserving trust, promoting progress II: principles and recommendations for oversight of an institution's financial interests in human subjects research. *Acad Med* 2003; **78**:237–45.
34. Weinfurt KP, Hall MA, Dinan MA, Dinan MA, DePuy V, Friedman JY, *et al.* Effects of disclosing financial interests on attitudes toward clinical research. *J Gen Intern Med* 2008; **23**:860–6.
35. Blumenthal D. Academic-industrial relationships in the life sciences. *N Engl J Med* 2003; **349**:2452–9.
36. Ellis PM. Attitudes towards and participation in randomised clinical trials in oncology: a review of the literature. *Ann Oncol* 2000; **11**:939–45.
37. Verheggen FW, Nieman F, Jonkers R. Determinants of patient participation in clinical studies requiring informed consent: why patients enter a clinical trial. *Patient Educ Couns* 1998; **35**:111–25.